CONDITIONAL PETITION FOR EXTENSION OF TIME

If any extension of time for this response is required, Applicants request that this be considered a petition therefore. Please charge the required fee to Deposit Account No. 14-1263.

ADDITIONAL FEES

Please charge any further insufficiency of fees, or credit any excess to Deposit Account No. 14-1263.

REMARKS

Claims 2-10 are pending in the application.

All claims have been rejected as allegedly being obvious over the combined disclosures of Matsumura, Ikekawa, Shoji in view of Ziolokowsky.

PRIOR ART REJECTIONS

Applicants respectfully request withdrawal of the prior art rejection in view of, *inter alia*, the references teaching away from each other as well as the claims, and for not being enabling for the claimed subject matter.

General Comments

Examiner cites Matsumura, Ikekawa, Shoji as showing that the compounds were "old and well known in combination with various pharmaceutical carriers and excipients in a dosage form."

Respectfully, these cited references do not disclose the use of any alkylated or acylated mono- or oligosaccharides with any pharmaceutically acceptable excipient. For example, Matsumara performs experiments on nutrient agar plates. This cannot reasonably be viewed as a pharmaceutically acceptable excipient.

Similarly, Ikekawa performs studies on agar plates or with liquid m dia, neither of which can be reasonably viewed as pharmaceutically acceptable excipients. For *In vivo*

studies, Ikekawa injects mice intraperitoneally. All of these disclsosure are far removed from topical administration. Therefore, the reference cannot reasonably be viewed as providing guidance to persons with skill in the art who seek to arrive at the claimed subject matter.

Shoji discloses oligosaccharides that are both *sulfated* and acylated, and therefore distinct in structure from those used in the claimed formulations. In addition, these compounds are formulated for oral administration to prevent HIV infection. This specific and narrow use of this class of compounds suggests that they are likely to be reverse transcriptase inhibitors. Therefore, the structure and function of Shoji's sulfated oligosaccarides are beyond the scope of the claimed subject matter.

Further distinctions are discussed below.

Ikekawa et al.,

A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 USPQ 303 (Fed. Cir. 1983). When analyzed in this context, Ikekawa teaches away from the claimed subject matter.

As generally stated in the paragraph bridging pages 2894 and 2895, Ikekawa's compounds show high cytotoxicity in various toxicity assays; e.g., mammalian cell cultures, bacteria, and plant cells. No predictable efficacy with respect to the compound's structure or dosage is disclosed. Persons of ordinary skill would likely conclude that use of such compounds in humans would not be feasible due to the almost certain cytotoxic effects.

"A reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant." *In re* Gurley, 31 USPQ2d 1130 (Fed. Cir. 1994). In other words, if a reference would have discouraged the ordinary skilled artisan from taking a particular research path, then the reference teaches away from that particular path's results.

Such contrary teachings would not motivate one in the art to combin it with other references, let alone Sh ji, Matsamura and Ziolokowsky.

It is respectfully suggested that Ikekawa cannot be reasonably combined with the other references to teach or suggest the claims. In contrast to Examiner's assertions, there are no pharmaceutically acceptable excipients disclosed. Nor is there even a rational basis to expect that these compositions would be useful for improving skin and hair care.

As discussed below, Ikekawa's deficiencies cannot be cured by combination with the other references.

On this basis alone, the rejections under § 103(a) may be withdrawn.

Matsamura et al.,

At best, Matsamura reiterates a suggestion of antimicrobial activity as in Ikekawa. However, Matsumara also indicates that gram-negative bacteria are not greatly effected. See text under Table 6. Further, the fungus Candida albicans, also seems to be relatively resistant. See Table 5, where most compounds are ineffective even at the highest concentrations present.

Further, in contrast to Examiner's assertions, there is no teaching of any pharmaceutically acceptable excipient, let alone any indication that the compounds can be safely used on skin and hair, let alone therapeutically used.

It is not clear what teaching or suggestion Examiner extracts from Matsamura, other than these compounds may be effective against some bacteria when tested on an agar dish. Matsamura actually provides less relevant disclosure than Ikekawa, thus, combining their disclosures does not come closer to the claims than does Ikekawa alone.

Shoji Cannot Fairly be Combined With Matsumara and Ikekawa

Ikekawa's compounds demonstrate a broad range of cytotoxicity –bacteria and fungi, plant cells, and mammalian cells. In contrast, Shoji discloses a formulation that humans are to take orally and thus, have distributed throughout the body. Applicants submit that based on Matsumara and Ikekawa's disclosure of alkylated oligosaccharides having a broad, non-specific cytotoxicity, these references would not be combined with Shoji because th ir respective disclosures teach away from one another.

It is well-settled law that it is improper to combine references where the references teach away from their combination. *In re Grasselli*, 218 USPQ 769, 779 (Fed. Cir. 1983).

On this basis, the rejections under § 103(a) may be withdrawn.

Examiner's citing of Shoji is apparently based on the presumption that Shoji's sulfated compounds are sufficiently similar in structure to those used in the claimed compositions, or those disclosed by Matsamura and Ikekawa.

However, in summarizing the prior art, Shoji himself refers to unsulfated oligosaccharides that lack sulfate groups as "only being esterified." See Shoji, col. 1, lines 30-32. Applicants submit that if Shoji expressly distinguishes these groups of compounds, then persons of skill in the art would not likely find structural or functional equivalence between the two based on the cited references.

A *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. See MPEP § 2144.09. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, *in the expectation that compounds similar in structure will have similar properties*." In re Payne, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979) (Emphasis added).

It is respectfully brought to Examiner's attention that Shoji's compounds are sulfated. This modification is, without more, sufficient to defeat the presumption of similarity. For example, *In re Grablak*, substitution of a thioester group for an ester group in an herbicidal safener compound was not suggested by the prior art and not found sufficient to render the claims obvious. *In re Grablak*, 226 USPQ 871 (Fed. Cir. 1985).

Examiner provides no rationale for alleging the similarity between the distinct groups of compounds. Thus, applying Shoji as a reference is tantamount to a mere allegation f similarity of th groups of compounds without any evidence that persons of skill in the art would have been able to use Shoji to cure the deficiencies in Matsumara and

Ikekawa. In accordance, this unsupported presumption is not sufficient to maintain a *prima facie* case of obviousness. *In re Jones*, 21 USPQ 2d, 1941, 1943-44 (Fed. Cir. 1992).

This is further supported by the holding in *Grabiak*, where the court held that "there must be adequate support in the prior art for the ester/thioester change in structure, in order to complete the PTO's prima facie case." *In re Grabiak* at 872. Grabiak is similar to the facts of this rejection to the extent that the Examiner in *Grabiak* viewed the distinction between thioesters and esters were obvious in the art. Examiner in the instant case seems to similarly believe that a sulfated oligosaccharide is not significantly different than an oligosaccharide. It is respectfully suggested that as in *Grabiak*, Examiner's rationale is insufficient to maintain the rejection.

Perhaps Examiner's support for his presumption is derived by drawing an analogy between the cytotoxic effects shown by Matsumara and Ikekawa and the purported anti-HIV effects of Shoji's compositions. However, these properties are too distinct to allow the analogy.

For example, Shoji demonstrates a narrow effect of the sulfated oligosaccharides on HIV, a retrovirus. However, there is no suggestion in Ikekawa or Matsamura that their compounds would be useful as anti-retroviral compounds, or be effective against any virus. Conversely, Shoji does not disclose the desirability of his compounds for any other purpose. Therefore, there is no clear motivation to combine the teachings of these references.

In addition, persons of skill in the art know that retroviruses have a life-cycle that is very different from other viruses, let alone other life forms.

Therefore, there is no rationale for expecting that substituting the modified mono and oligosaccharides in the claimed compositions with Shoji's sulfated oligosaccharides would result in dermatological or cosmetological compositions having the desirable properties.

In fact, Shoji discloses virtually every manner of administ ring the compound except topically. Shoji discloses intravenous, ral, intramuscular, intraperiton al and intrarectal.

See col. 18, lines 12-18. This is because, in part, retroviruses generally are transmitted through blood, and are released into the bloodstream during infection.

In brief, established case law and the MPEP indicate that Shoji's compounds should not be presumed similar to those of Matsumara and Ikekawa. In support of this is the fact that the testing methods used for these different compounds are sufficiently unrelated that they cannot be presumed to have similar properties. In fact there cannot reasonably be a motivation to combine these references.

Ziolkowski et al. Does not Cure the Deficiencies in the Primary References

It is well established that a proper reference under 35 USC §§102 or 103 must be enabling in the sense of 35 USC §112, ¶1. It is suggested that the Ziolkowski reference is not enabling to that extent. Pertinent is the following quote from *In re Le Grice*, 133 USPQ 365, 374 (CCPA 1962):

> "[T]he proper test of a description in a publication as a bar to a patent as the clause is used in section 102(b) requires a determination of whether one skilled in the art to which the invention pertains ***could take the description of the invention in the printed publication and combine it with his own knowledge of the particular art and from this combination be put in possession of the invention*** on which a patent is sought. [Emphasis added.]"

See also, *In re Hoeksema*, 158 USPQ 596, 601 (CCPA 1968), wherein the Court stated:

> "While *In re Le Grice* was bottomed on an issue arising under 35 U.S.C. 102 where the reference was a 'printed publication,' that test, in our view, is also properly applicable to issues arising under 35 U.S.C. 103."

The disclosure in Ziolkowski cannot reasonably provide an enabling reference, even for what Examiner purp rts the abstract as teaching. For example which alkyloligoglucoside is preferr d? How much? Are they all qually potent?

Is it Examiner's suggestion that persons with skill in the art would know to use one of Ikekawa's or Matsumara's compounds in Ziolkowski's method? If so, which ones? Would person's with ordinary skill in the art know to employ Shoji's sulfated oligosaccharides?

There is no clear answer, to these questions and in view of the numerous contrary teachings one could not have a reasonable expectation of success in trial and error.

In addition, Examiner over interprets Ziolkowski by assuming that the alkyloligogucoside is the active agent, or a key active agent or is functioning in an antimicrobial capacity in the composition. Ziolkowski does not teach or suggest that alkyloligoglucosides should or may be used away from the context of the entire composition of esters, natural triglycerides and a high content of unsaturated fatty acids.

Further, there is not a word in Ziolkowski that his composition has antimicrobial activities. Examiner has improperly read this into the abstract.

In brief, Ziolkowski not teach the claimed formulations or properties, nor does he or the Examiner provide evidence that such a composition inherently possesses these properties.

In view of Ziolkowski's clear nonenabling disclosure, its combination with Matsumara, Ikekawa and/or Shoji do not teach or suggest each claim limitations. Therefore, Applicants respectfully request withdrawal of all rejections under § 103(a).

Respectfully Submitted,

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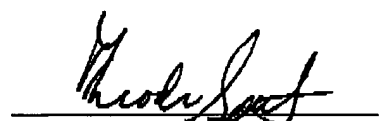

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